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# Myopericarditis after the Pfizer mRNA COVID-19 Vaccine in Adolescents

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Reports have emerged of myocarditis and pericarditis predominantly after the second dose of the COVID-19 mRNA vaccine. We describe 13 patients 12-17 years of age who presented with chest pain within 1 week after the second dose of the Pfizer vaccine and were found to have elevated serum troponin levels and evidence of myopericarditis.

Abbreviations

Left Ventricle (LV)

Ejection Fraction (EF)

Cardiac MRI (CMR)

Late Gadolinium Enhancement (LGE)

Intravenous Immunoglobulin (IVIG)

The FDA extended the emergency use authorization of the Pfizer-BioNTech mRNA COVID-19 vaccine for adolescents 12 through 15 years of age on May 10, 2021[1]. Following authorization large numbers of adolescents across the country began to receive immunization. As of June 21, 2021, 98,008 adolescents 12 through 15 years of age and 69,489 adolescents 16 and 17 years of age in Washington state completed the 2-dose schedule of mRNA COVID-19 vaccine [2].

Reports of post-COVID-19 vaccine myocarditis and pericarditis have emerged , particularly after the second dose of the mRNA vaccines. Initial cases were noted predominantly in male adolescents and young adults in the Israeli military[3]. Subsequently, U.S. institutions have reported 7 cases in adolescents over 16 years old[4] and 7 cases in young adults [5]. As the age range of eligibility for the COVID-19 vaccine broadened in Washington state we have cared for a cohort of younger patients with post-vaccine myopericarditis. We describe clinical and cardiac MRI (CMR) findings for 13 patients 12 through 17 years of age cared for in our center.



## Methods

We performed a retrospective electronic medical record review. Institutional Review Board approval was obtained. Inclusion criteria were patients younger than 18 years of age presenting with severe chest pain and signs of myopericarditis within 1 week of receiving the second dose of Pfizer COVID-19 vaccine from April 1, 2021 to June 21, 2021.

## Results

Clinical and laboratory findings are shown in Table I. We identified 13 patients with myopericarditis. Median age was 15 years (range, 12-17 years). Most patients were male (N=12, 92%). The majority of patients were white and non-Hispanic (N= 10, 76.9%). Median time to presentation from the second dose of the Pfizer COVID-19 mRNA vaccine was 3 days (range 2-4 days). Per inclusion criteria all patients had sudden onset, intense and persistent chest pain. The chest pain was not exacerbated by movement or activity. The most common accompanying symptoms were shortness of breath (N=6, 46.2%), tactile temperature (N=5, 38.5%), and myalgias (N=4, 30.7%).

All patients had elevated serum troponin levels (median 9.18 ng/mL, range 0.65-18.5). Median serum B-natriuretic peptide level was 37.5 pg/mL (range 7-87pg/mL). CRP was elevated in patients in whom CRP was measured (N=10, median 3.7 mg/dL, range 1.4-6.5 mg/dL) COVID-19 nucleocapsid IgG antibody was measured in 9 patients and was negative in all.

Cardiac testing and results are shown in Table II. Nine patients had an abnormal EKG, with the most common finding being ST segment elevation. All patients had an echocardiogram on admission; 11/13 patients had normal left ventricular (LV) systolic function; 2 patients demonstrated mildly reduced LV systolic function as well as regional left ventricular wall motion abnormalities. The median left ventricular ejection fraction (LVEF) was 60% (range 45-69%, normal defined as >55%). No patients had significant pericardial effusion. One patient had an incidental finding of bicuspid aortic valve without regurgitation or stenosis.

All patients had cardiac MRIs (CMR) within 1 week of presentation. All CMRs performed were abnormal showing late gadolinium enhancement (LGE) in a patchy subepicardial to transmural pattern with predilection for the inferior left ventricle free wall (Figure). Additionally, all CMRs had evidence of edema in corresponding segments by T2

imaging and fulfilled the Lake Louise Criteria[6] for myocarditis. Left ventricular regional wall motion abnormalities were noted in 2 patients; CMR based LV systolic function was mildly decreased in 8 patients. The CMR LVEF ranged from 46-61%, median 53%. No significant pericardial effusions were seen on CMR.

All patients received scheduled doses of nonsteroidal anti-inflammatory agents (ie, ibuprofen every 8 hours with dose dependent on patient weight). Three patients received intravenous immunoglobulin (IVIG), 2 of whom were the patients with decreased left ventricular function by echocardiography. These 2 patients also received corticosteroids per our institutional pathway for treatment of myocarditis. One patient had isolated premature ventricular contractions on telemetry; no other patient had evidence of arrhythmia. Median hospital length of stay was 2 days (range 1-4 days) with no ICU admission, significant morbidity, or mortality. All patients had resolution of chest pain and falling serum troponin level prior to discharge.

## DISCUSSION

We report 13 adolescents with myopericarditis after the second dose of the Pfizer mRNA COVID vaccine. This cluster of cases was identifiable as age of vaccination for eligibility broadened with emergency use authorization by the FDA. We are the only free-standing children's hospital in Washington state and serve as a tertiary referral institution. To our knowledge, at least 3 other cases in this age group have been cared for at other hospitals in the state. Using these numbers and Washington state Department of Health data on immunization [2] we estimate a possible incidence of 0.008% in adolescents 16-17 years of age and 0.01% in those 12 through 15 years of age following the second dose.

All patients had evidence of myocardial inflammation and edema on CMR, similar to findings in limited case series of adults with post-COVID-19 vaccine myocarditis [7]. Although all patients' symptoms resolved rapidly, the CMR findings indicate the potential for myocardial fibrosis and unknown long-term impact. Accordingly, we are following the AHA/ACC acute myocarditis recommendations for exercise restrictions of up to 6 months and long-term cardiac surveillance[8]. Additionally, follow up CMR is planned for all patients at 3 months, which may allow us to shorten the period of exercise restriction.

We speculate that a hyperimmune response to the second dose of the vaccine is plausible. Children have demonstrated a more robust immune response to SARS-CoV-2 infection than adults as observed with multisystem inflammatory syndrome in children (MIS-C)[9]. For noninferior immunogenicity it is possible the interval between doses 1 and 2 should be longer in children than in adults or that a reduction in content of dose 2 would be appropriate in people less than 18 years of age.

It is noteworthy that 2 of our cases had a family history of myocarditis in first degree relatives. There is evidence that genetics may play a role in the susceptibility of patients to myopericarditis[10]. This predisposition may increase the likelihood of inflammation and cardiac effects after the vaccine.

The Pfizer Phase 2/3 clinical trial included only 754 participants in the 16 and 17 year old age group and 2,260 in the 12 to 15 year old age group. Approximately 50% were male [11]. As noted, we have estimated the incidence of myopericarditis in the younger group near 0.01% of those receiving second dose vaccines. Due to reporting issues, delays, and early inability of practitioners to associate myopericarditis with vaccine this value is likely an underestimate. Additionally, our Washington state Department of Health vaccine data for these age groups are

not segregated by sex. This adverse event would likely not be detected in the small population of males who received study vaccine and highlights the need for aggressive post-authorization surveillance.

Although a causal relationship between vaccine receipt and development of myopericarditis cannot be concluded from a case series, clustering in time as well as the uncommon occurrence of myopericarditis and the rapid resolution of symptoms and findings made this likely to be a unique vaccine related event. Identification of myopericarditis as an adverse event should have high priority during investigations before and after authorization of COVID-19 vaccines and be considered by policy makers in the risk/benefit ratio in adolescents and children.

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Figure Legend.

Figure 1. Short axis Cardiac MRI image with arrow showing delayed enhancement in the inferior and inferolateral basal segments of the left ventricular free wall

Table 1. Demographics Features and Clinical Findings in Adolescents following Pfizer mRNA COVID-19 Vaccine

| Patient # | Demographics | | | Clinical Information | | | Lab Testing | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Age | Sex | Race | Length of stay (days) | Days from vaccine to presentation | Other symptoms | Peak troponin ng/mL (normal < 0.05ng/mL) | Peak BNP pg/mL (normal <55 pg/mL) | Peak CRP mg/dL (normal < 0.08 mg/dL) | COVID IgG Nucleocapsid ab testing |
| 1 | 16 | M | White Non-Hispanic | 1 | 2 | Fever, chills, myalgias, headache, shortness of breath | 8 | 15 | 4.3 | Negative |
| 2 | 16 | M | Asian Non-Hispanic | 1 | 2 | Fever, myalgias | 11.1 | 28 | 3.5 | Not tested |
| 3 | 16 | M | White Non-Hispanic | 3 | 3 | Myalgias, headache | 10.9 | <10 | 3.6 | Negative |
| 4 | 17 | M | American Indian/Alaska Native Non-Hispanic | 1 | 3 | Fever, malaise | 9.18 | 14 | -- | Negative |
| 5 | 15 | M | White Non-Hispanic | 2 | 2 | Myalgias, shortness of breath | 4.95 | 13 | 5.5 | Negative |
| 6 | 15 | F | White Non-Hispanic | 1 | 3 | Vomiting | 0.65 | 7 | 1.4 | Negative |
| 7 | 15 | M | White Non-Hispanic | 3 | 3 | Fevers, shortness of breath | 9.12 | 74 | 3 | Negative |
| 8 | 15 | M | White Non-Hispanic | 3 | 3 | Chills | 13.2 | 87 | 6.2 | Negative |
| 9 | 12 | M | White Non-Hispanic | 2 | 3 | None | 13 | 37 | -- | Negative |
| 10 | 14 | M | White Non-Hispanic | 3 | 3 | Fever, headache | 18.5 | 66 | -- | Negative |
| 11 | 14 | M | Asian Non-Hispanic | 2 | 4 | Malaise shortness of breath | 6.08 | 55 | 3.7 | Not tested |
| 12 | 16 | M | White Non-Hispanic | 2 | 2 | Shortness of breath | 16.4 | 38 | 6.5 | Not tested |
| 13 | 15 | M | White Non-Hispanic | 2 | 3 | None | 7.89 | 86 | 3.4 | Not tested |

Table 2. Cardiac Testing Results and Treatment in Adolescents following Pfizer mRNA COVID-19 Vaccine

| Patient # | Cardiac Testing | | | | | | | Treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | EKG | Echocardiogram | | Cardiac MRI | | | | | | |
| | Findings | Left Ventricular Wall motion Abnormalities | LVEF (Normal ≥ 55%) | LVEF (Normal ≥ 55%) | Edema | LGE | Focal hypokinesis of left ventricle | IVIG | Corticosteroids | NSAIDs |
| 1 | Normal | N | 66 | 50.8 | Y | Y | N | N | N | Y |
| 2 | ST elevation | N | 59 | 51.1 | Y | Y | N | N | N | Y |
| 3 | ST elevation | N | 69 | 56.6 | Y | Y | N | Y | N | Y |
| 4 | ST elevation | N | 58 | 49.4 | Y | Y | N | N | N | Y |
| 5 | Normal | N | 58 | 52 | Y | Y | N | N | N | Y |
| 6 | Non specific T wave changes | N | 58 | 48 | Y | Y | N | N | N | Y |
| 7 | T wave inversion | N | 61 | 61 | Y | Y | N | N | N | Y |
| 8 | ST elevation | Y | 45 | 46 | Y | Y | Y | Y | Y | Y |
| 9 | Normal | N | 64 | 54 | Y | Y | N | N | N | Y |
| 10 | ST elevation | N | 62 | 55 | Y | Y | Y | N | N | Y |
| 11 | ST elevation | N | 60 | 58 | Y | Y | N | N | N | Y |
| 12 | ST elevation | Y | 53 | 58 | Y | Y | N | Y | Y | Y |
| 13 | Normal | N | 61 | 53 | Y | Y | N | N | N | Y |

Y= Yes

N= No